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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,333	02/21/2001	Lanfranco Callegaro	204,940	9321

7590 11/13/2007
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New York, NY 10017-5621

EXAMINER

FUBARA, BLESSING M

ART UNIT	PAPER NUMBER
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1618

MAIL DATE	DELIVERY MODE
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11/13/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/743,333	Applicant(s) CALLEGARO ET AL.	
	Examiner Blessing M. Fubara	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25-32 and 34-44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25-32 and 34-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Examiner acknowledges receipt of request for continued examination filed under 37 CFR 1.114, remarks and petition for revival of the application filed 6/26/07; and compliant amendment and remarks filed 8/10/07. Claims 25, 31, 32, 34 and 39-44 are amended after the decision of the BPAI of 02/26/07. Claims 25-32 and 34-44 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 6/26/07 and 8/10/07 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 25-32 and 34-44 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Valentini et al. (US 5,939,323).

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Valentini discloses “three dimensional biodegradable scaffolds of hyaluronic acid derivatives for tissue reconstruction and repair,” (column 4, lines 31-33) using the derivatives of HA, such as HYAFF (see Examples 1-3, 5 for the use of the HYAFF) as raw material to fabricate porous, degradable scaffolds for tissue repair and wound healing (See column 1, lines 64-67); and specifically discloses that the scaffolds can have virtually any size, thickness and shape having various porosities and pore sizes (column 4, lines 36-38) and which can be used for attachment of bioactive molecules (See column 2, lines 7-22). For Valentini, the most preferred hyaluronic acid derivative is hyaluronic acid esterified with a benzyl moiety (See column 2, lines 54-67) meeting claims 27-32 and 35-37. Valentini discloses that the scaffolds may be used for repair of bone defects, for treating non-healing fractures and osteoporetic lesions, for treating tooth and jaw defects and cartilage defects, for repair of defects and damage in skin, muscle and other soft tissues (column 7, lines 36-57 and column 8, line 1) and that in each of these cases, the scaffold is seeded with cells that would differentiate into the respective damaged tissues ((column 7, lines 36-57 and column 8, line 1). Valentini also discloses that “likewise, damage to visceral organs including liver damage, ... damage resulting from intestinal cancer or intestinal ulcer may be treated with the scaffolds of the invention. In these instances, the scaffolds can be seeded with cells such as ... intestinal cells,” (column 8, lines 1-6). The perforated membrane of the claims read on the porous scaffold of Valentini, which scaffold can also be a membrane.

Claims 34 and 39-44 are product by process claims and the requirement for fibroblasts, mesenchymal cells, mature cells and/or epithelial in the biological material is optional. However, Valentini specifically notes that the scaffold may/is seeded with precursor cells, for

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example, mesenchymal stem cells from bone marrow, periosteum, endosteum, etc, which are bone cell precursors, are seeded onto the scaffold in the case of bone repair where (column 7, lines 39-43). Furthermore, "morphological differentiation of intestinal cells" now recited in the amended claim 25 appears to be natural development within the seeded cells so that the intestinal cells seeded by Valentini on the scaffold must undergo the "morphological differentiation." Nonetheless, Valentini clearly recognizes and discloses that cells seeded onto the scaffold differentiate into the respective tissues as is described in column 2, lines 10-12 and 22; column 3, lines 15, 58; column 4, line 9; column 6, lines 31-38; column 8, line 10; column 10, lines 5, 64 and 65; and column 11, line 30.

Thus, Valentini provides HA matrices for the ingrowths of intestinal cells. In the alternate, one skilled in the art would understand the scaffold of Valentini to be single layer and porous or perforated membrane.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 25-32 and 34-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dorigatti et al. (WO 94/17837) in view of Valentini et al. (U.S. Patent 5,939,323).

Dorigatti provides a multilayer non-woven material comprising a layer coming in contact with the skin and that layer is made of materials selected from the group consisting of a derivative of hyaluronic acid, specifically a hyaluronic acid ester, and a perforated membrane compatible with cell growth on its surface (See p. 2, lines 16-34) with the layer comprising the hyaluronic acid derivative meeting a single layer in which cells are seeded because it is the perforated layer that is in contact with the skin (page 6, lines 14-21). Dorigatti teaches that the perforated membrane may include glycosaminoglycans (See p. 6, lines 13-29) and the non-woven tissue can be impregnated with pharmaceutically active compounds and be used in surgery because of its anti-adhesive properties (See p. 7, lines 16-28). The derivatives of hyaluronic acid is HYAFF (see Examples 1-7), which is the same hyaluronic acid derivative of the invention as gleaned from applicant's specification at page 6, line 26 and page 7, line 7, meeting claims 26-32 and 35-38. Claims 34 and 39-44 are product by process claims and the presence of cells other than the intestinal cells is optional.

Thus, with regard to claims 25, 34 and 39-44, the international publication provides the general teachings that cells can be grown on a single layer of hyaluronic acid esters and/or a perforated membrane comprising glycosaminoglycans and hyaluronic acid derivative. The material may be used in surgeries, where its anti-adhesive properties are required. Dorigatti is

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deficient in the sense, that the publication does not specify the type of cells, which may be grown on hyaluronic acid containing perforated membrane that is in contact with the skin or Dorigatti contemplates growing a variety of cells on hyaluronic acid containing perforated membrane that is in contact with the skin.

With respect to claims 26-32 and 35-38, Dorigatti teaches that hyaluronic acid esters are preferred in the layer contacting the skin (See p. 2, lines 30-34), and includes the esters of hyaluronic acid disclosed in U.S. 4,851,521 and comprising esters of hyaluronic acid with alcohols, sulfonic acids and neutral sulfates, among the hyaluronic acid esters used in the invention (See p. 4, lines 26-29). Furthermore, "morphological differentiation of intestinal cells" now recited in the amended claim 25 appears to be natural development within the seeded cells so that the intestinal cells seeded by Dorigatti on the perforated layer comprised of HYAFF must undergo the "morphological differentiation."

But, Valentini discloses seeding or growing intestinal cells on HYAFF (column 7, line 36 to column 8, line 17) and thus provides the deficiency of Dorigatti.

Therefore, a person of ordinary skill in the art, taking the references together would grow intestinal cells or any other cells on the perforated membrane layer of Dorigatti since Valentini discloses that intestinal cells can grow and differentiate on HYAFF matrices. Therefore the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

7. Applicant's arguments filed 6/26/07 have been fully considered but they are not persuasive.

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A) Regarding applicant's argument that Valentini's three-dimensional scaffold is not a "bi-dimensional scaffold based on hyaluronic acid derivatives in the form of membranes that do not have interconnected pores (perforated membranes), or do not have pores at all (continuous membranes)," a) it is noted that the perforated membrane of the claims is porous and would read on porous matrix or spongy matrix, b) a perforated matrix would necessarily have interconnecting lines without which will be one big hole, c) a continuous membrane is an alternative to perforated membrane and the prior art does not have teach both alternatives to meet the claims.

B) Regarding Dorigatti and the multi-layer material containing hyaluronic acid, it is brought to applicant's attention that it is the one surface layer in contact with the skin that is comprised of the hyaluronic acid according to at least page 2, lines 19-30 and page 6, lines 13-16. Applicant's single perforated layer reads on Dorigatti's perforated membrane layer comprising hyaluronic acid, which is the layer in contact with the skin and upon which is seeded cells. Even the perforated membrane layer of hyaluronic acid is stuck to the other layer, the membrane upon which the cells are seeded is a single layer. Valentini provides a teaching that intestinal cells can be seeded on hyaluronic acid matrix or that hyaluronic acid matrices support growth of intestinal cells. The rejection of the claims is based on the combination of Valentini and Dorigatti while applicant appears to be arguing against the references individually, but one cannot show nonobviousness by attacking the references individually where the rejections are based on combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

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C) Regarding the growth of intestinal cells on “bi-dimensional scaffolds in the form of membranes,” and which also “undergo morphological differentiation with the formation of microvilli on their surface,” it is noted that perforated membrane or scaffold of the invention is not exclusionary to bi-dimensional membrane or scaffold and intestinal cells seeded on hyaluronic acid matrix as described by Valentini must undergo morphological differentiation as the intestinal cells of the invention that are seeded on hyaluronic acid membrane or scaffold.

D) Regarding higher alkaline phosphatase activity for the cells on applicant's membranes v. many other types of scaffold, it is noted that applicant's scaffold reads on the scaffold of Valentini, which is a single layer matrix of hyaluronic acid in the form of a spongy matrix (Example 1) and also the single perforated layer of Dorigatti, which is in contact with the skin and which is comprised of hyaluronic acid derivative (page 2, lines 19-30 and page 6, lines 13-16).

E) The Example at page 7 and the figures of the filed specification are not in the claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Blessing Fubara
Patent Examiner
Tech. Center 1600

A handwritten signature in black ink, appearing to read "Blessing Fubara", is written over the printed name and title.